

was similar, whereas the prevalence of men not co-infected decreased (1.93-0.46%). This suggests that HIV-1 infection associated with parenteral transmission has been stable despite a dramatic reduction in the sexual transmission of HIV-1.

AIDS. 2004; 18(17): 2339-41.

CO-INFECTION BY HIV-1 AND SCRUB TYPHUS MAY LEAD TO DECREASED VIRAL LOAD AND PREFERENTIAL SUPPRESSION OF X4 VIRUSES

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Background: Scrub typhus (*O. tsutsugamushi*) infection of HIV-positive patients can be accompanied by a decrease in HIV load. Transfer of plasma from scrub typhus patients to HIV-infected individuals also results in a drop in viral load. The mechanism of suppression is unclear but may involve induction of inhibitory substances like chemokines or cross-reactive antibodies.

Methods: We tested sera from HIV-negative scrub typhus patients for its ability to inhibit replication of CCR5- (R5) and CXCR4-specific (X4) strains of HIV *in vitro*. We performed genotypic analyses to determine the coreceptor usage of virus obtained from HIV-infected individuals infused with plasma from scrub typhus patients. A mathematical model was used to quantitate the proportion of HIV using each coreceptor and mixed-effects analyses were used to examine the relationship between viral load, coreceptor usage, and chemokine concentration.

Results: *In vitro* replication of HIV was inhibited 2 to 10-fold by addition of sera from scrub typhus patients; this effect was limited to X4 strains. Although depletion of chemokines had no impact on HIV replication, depletion of antibody abrogated the serum's inhibitory effect. *In vivo*, passive transfer of plasma from scrub typhus-infected patients into HIV-infected individuals caused a substantial decrease in viral load for 7 of 10 recipients. This reduction in HIV RNA level was accompanied by a significant shift in the viral population from X4 to R5 strains ($p=0.0008$). Patients who showed no drop in HIV load were infected by virus that was solely R5. No association was seen between changes in viral load and serum chemokines. Viral load and coreceptor usage did not change in 3 patients who received placebo infusions of saline.

Conclusions: These data suggest that scrub typhus infection may induce antibodies or other soluble molecules that inhibit X4 strains of HIV. Elucidating the mechanism of suppression of X4 virus is relevant to treatment and vaccine design.

XV International AIDS Conference. Bangkok, Thailand. 11-16 July 2004.
